Korelasi antara Kadar *C-Reactive Protein* dengan *Grading* Radiologik pada Osteoartritis Lutut

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ABSTRAK

Pendahuluan. Beberapa penelitian telah menggambarkan bahwa respons fase akut dapat terjadi pada osteoartritis, yang mendukung bahwa inflamasi sistemik l*ow grade* mungkin terdapat pada penderita osteoartritis.
Bahan dan cara kerja. Penelitian ini bertujuan untuk mengukur kadar *c-reactive protein* penderita osteoartritis sendi lutut, menentukan grading radiologik penderita osteoartritis lutut menurut klasifikasi Kellgren-Lawrence, dan menentukan hubungan antara kadar *c-reactive protein* dengan *grading* radiologik penderita osteoartritis sendi lutut. Penelitian observasional ini menggunakan desain potong lintang dengan 65 sampel wanita pascamenopause penderita osteoartritis sendi lutut dengan rentang usia antara 50-70 tahun.
Hasil. Dari 65 sampel; ditemukan sebanyak 28 (43%) sampel osteoartritis *grade* <3 dengan kadar *c-reactive protein* antara 0,2–1,0 mg/dl (0,54±0,23 mg/dl), 22 (34%) osteoartritis *grade* 3 dengan kadar *c-reactive protein* antara 0,3–1,4 mg/dl (0,70±0,33 mg/dl) dan 15 (23%) osteoartritis *grade* 4 dengan kadar *c-reactive protein* antara 0,3–1,3 mg/dl (rata-rata 0,80±0,26 mg/dl). Kadar *c-reactive protein* sampel secara keseluruhan adalah 0,2-1,4 mg/dl (rata–rata 0,65±0,29 mg/dl). Terdapat hubungan antara kadar *c-reactive protein* dengan *grading* radiologik pada osteoartritis sendi lutut, dengan p=0,04, korelasi Spearman rho=0,349 dan α=5%. Kadar *c-reactive protein* pada *grade* < 3, *grade* 3 dan *grade* 4 saling tumpang tindih sehingga tidak dapat digunakan untuk menentukan *grading* radiologik osteoartritis.
Simpulan. Tidak terdapat korelasi antara kadar *c-reactive protein* dengan *grading* radiologik pada osteoartritis sendi lutut. Terdapat kecenderungan pada osteoartritis sendi lutut dengan *grade* lebih tinggi untuk memiliki kadar *c-reactive protein* lebih tinggi pula.

Kata kunci : c-reactive protein, osteoartritis sendi lutut, *grading* radiologik

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The Correlation between Level of C-Reactive Protein and Radiographic Grading of Knee Osteoarthritis

ABSTRACT

Introductions. Several studies have shown that the acute phase response may take place in osteoarthritis, suggesting that low grade systemic inflammation may be present in patients with osteoarthritis.

Materials and methods. This study was aimed to measure the c-reactive protein level of knee osteoarthritis, to determine radiographic grading of knee osteoarthritis according to Kellgren-Lawrence grading, and to determine correlation between level of c-reactive protein and radiographic grading of knee osteoarthritis. This study used observational cross sectional design. Samples were 65 postmenopausal women with clinical knee osteoarthritis, aged 50 to 70 years old. Clinical and radiologic diagnoses of knee osteoarthritis were determined by clinical and radiographic examination with AP weight bearing position. Grade <3, grade 3 and grade 4 were radiographic grading of knee osteoarthritis according to Kellgren-Lawrence classification.

Results. From 65 samples, 28 (43%) samples had grade < 3 with level of c-reactive protein 0.2-1.0 mg/dl (0.54±0.23 mg/dl), 22 (34%) samples had grade 3 with level of c-reactive protein 0.3-1.4 mg/dl (0.70±0.33 mg/dl) and 15 (23%) samples had grade 4 with level of c-reactive protein 0.3 -1.3 mg/dl (0.80±0.26 mg/dl). The cumulative of level of c-reactive protein was 0.2-1.4 mg/dl (0.65±0.29 mg/dl). There is correlation between level of c-reactive protein and radiographic grading of knee osteoarthritis (p=0.04), with Spearman rho correlation of 0.349 and α=5%. The level of c-reactive protein in grade <3, grade 3 and grade 4 overlaps, so the level of c-reactive protein could not be used to determine radiographic grading of knee osteoarthritis.

Conclusions. There is no correlation between level of c-reactive protein and radiographic grading of knee osteoarthritis, there is a tendency that the level of c-reactive protein is higher in high grade knee osteoarthritis.

Keywords: c-reactive protein, knee osteoarthritis, radiographic grading

Introduction

Osteoarthritis (OA) is a disease of complex etiology that results in loss of normal function due to breakdown of articular cartilage. A consensus definition comes from a workshop of American Academy of Orthopaedic Surgeons in June 1995: "Osteoarthritic disease is a result of both mechanical and biologic events that destabilize the normal coupling of degradation and synthesis of articular cartilage chondrocytes and extracellular matrix, and subchondral bone.[1,2]

Prevalence of OA in population worldwide is high. It is estimated that by 2025 years, OA and other joints disorder will rank 25% of all disability and become world socioeconomic problems. Prevalence rate of OA in Indonesia in patients aged more than 15 years old are 15.5% in male and 13.7% in female.[3-6]

At one session of American College of Rheumatology Annual Meeting 1999 was done debate and discussion about OA pathogenesis and resulted in 52% who believed OA as inflammation process, while 48% believed that OA is pain syndrome. Most believed that degenerative and inflammation took role in OA pathogenesis. [7]

Several studies have shown that acute phase response may take place in OA, suggesting that low grade systemic inflammation may be present in patients with OA.[8,9] Spector et al.,[10] have shown level of c-reactive protein (CRP) to be higher in women with Kellgren-Lawrence grade above 2 knee OA. Takahashi et al.,[11] have shown correlation between radiographic grading and biochemical markers for arthritis of knee OA such as level of CRP.

Study about correlation between level of CRP and radiographic grading of knee OA has never been done in Indonesia and OA pathogenesis is still controversial, so this study is necessary and important. Moreover, since there is correlation between level of CRP and radiographic grading of knee OA, we believed level of CRP to be predictor of inflammation progress in knee OA while radiographic grading to be predictor of the severity of knee OA.

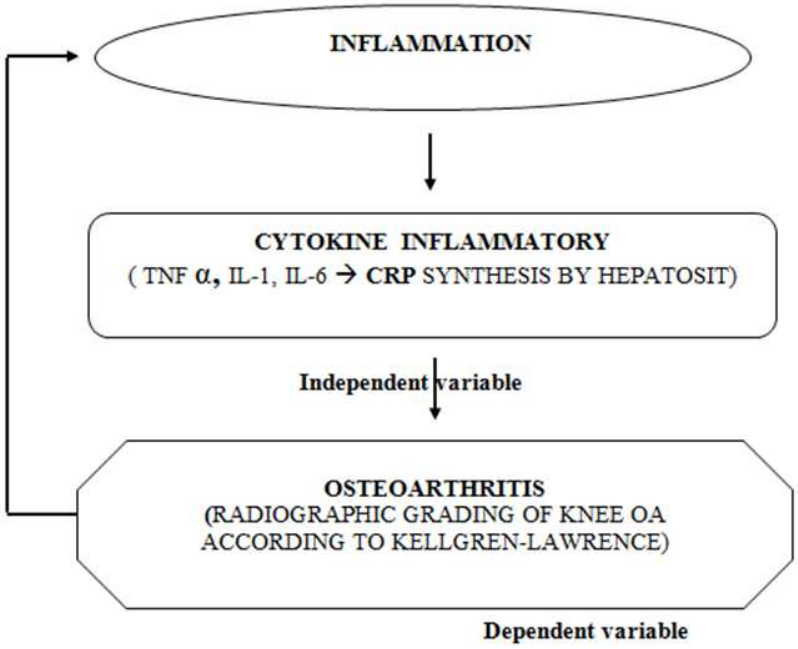

Figure 1. Conceptual framework

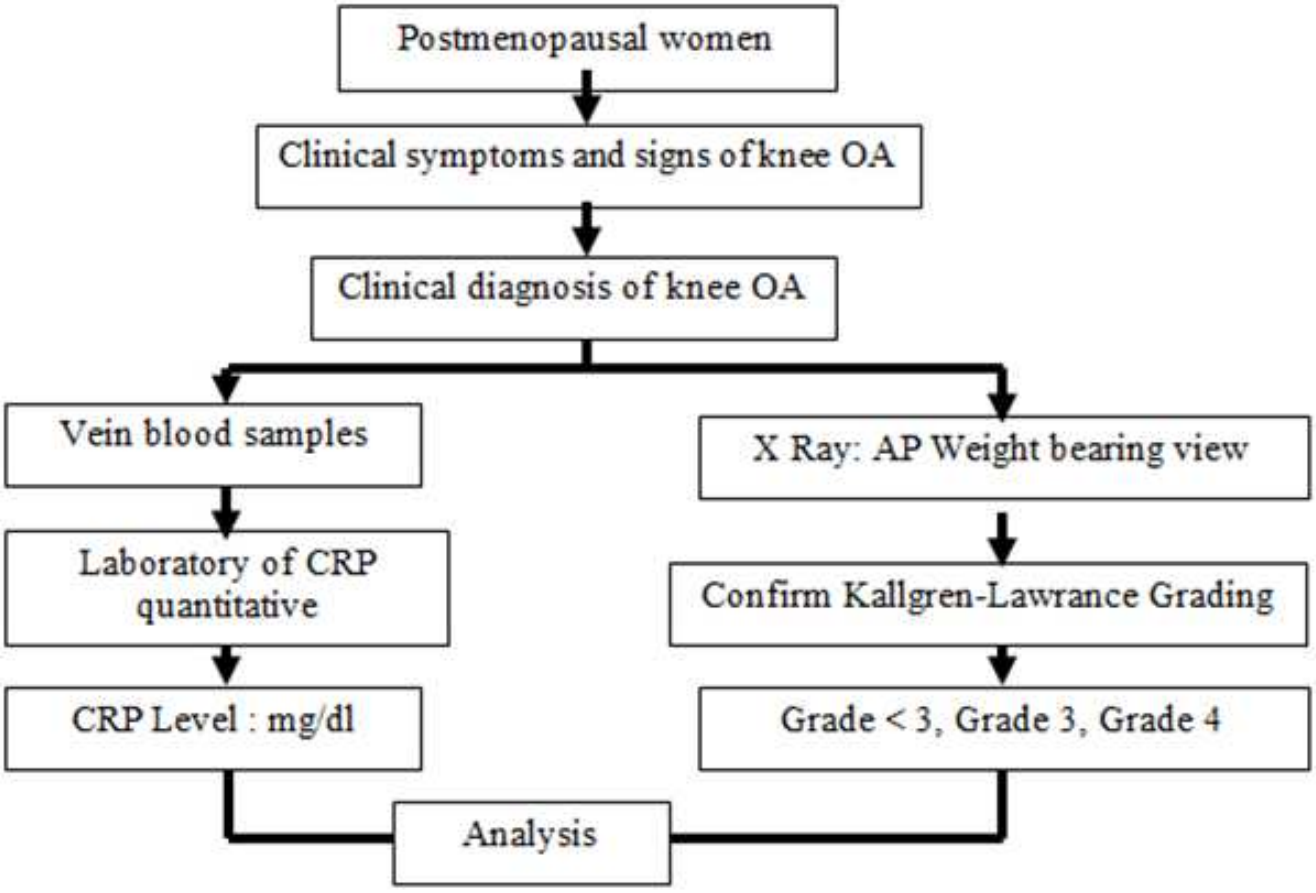

Figure 2. Working algorithm

The aims of this study are to measure level of CRP of knee OA, determine radiographic grading of knee OA according to Kellgren-Lawrence grading and determine correlation between level of CRP and radiographic grading of knee OA.

Materials and methods

Method of this study was observational cross sectional design. Inclusion criteria were postmenopausal Indonesian women clinically with clinical diagnosis of knee OA who agreed to participate in the study. Exclusion criteria were rheumatoid arthritis, extensive trauma, fractures, burns, bacterial or purulent meningitis, osteomyelitis, infectious post-operative complication, post-transplant rejection, severe viral and bacterial infections, acute myocardial infarction, tumors and diabetes mellitus.[12,13]

The samples were 65 postmenopausal women with clinical knee OA, range of age was 50-70 years old and met study criteria. Clinical and radiologic diagnosis of knee OA were determined by clinical and X-ray examination with AP weight bearing position. Grade < 3, grade 3 and grade 4 were radiographic grading of knee OA according to Kellgren-Lawrence classification. Clinical diagnosis were knee pain plus at least three of six: age > 50 years, stiffness ≤ 30 minutes, crepitation, bony tenderness, bony enlargement, and/or no palpable warmth.[14,15] Knee radiographs were evaluated with Kellgren-Lawrence grading scale.[11,16]

CRP was assayed by Cobas integra 400 plus as an in-hospital routine laboratory procedure (Laboratory of CRP quantitative). Conceptual framework was shown in figure 1 while algorithm of the in figure 2.

Data were calculated and hypothesis analysis were done Spearman correlation test and furthermore analysis. After identification level of CRP and radiographic grading according to Kellgren-Lawrence grading of knee OA, the analysis continue with table and graphic form.

Results

During October 2005 until May 2006 in Dr. Wahidin Sudirohusodo Hospital, Makassar, 65 patients fulfill the study criteria. Samples group were divided according to age, level of CRP, and radiographic grading of knee OA (Grade < 3, grade 3, and grade 4).

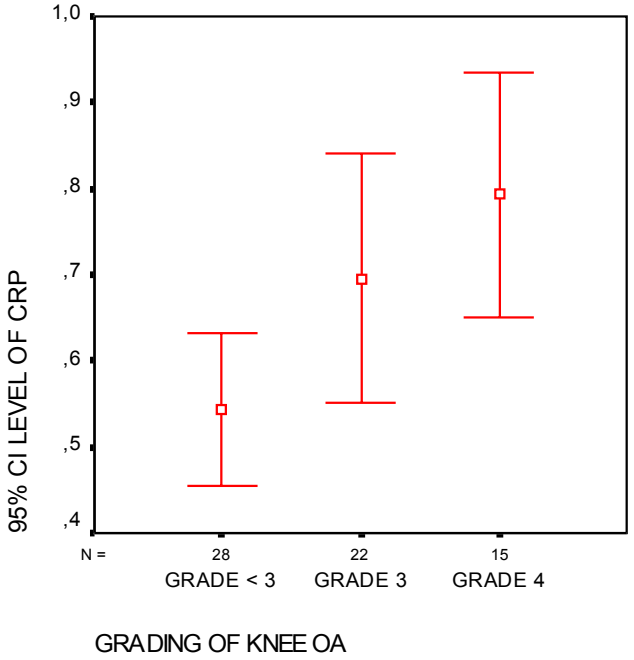

Figure 3. Description according to level CRP and radiographic grading at the sample

Table1 showed characteristic of the sample according to age, level of CRP and radiographic grading of knee OA. The cumulative of level of CRP was 0.2-1.4 mg/dl, mean 0.65 ± 0.29

There was a tendency for level of CRP to be higher in high than low grade knee OA. The correlation between the level of CRP and radiographic grading of knee OA was statistically significant ($p = 0.04$, Spearman rho correlation = 0.349, $\alpha = 5\ \%$). However, the levels of CRP overlapped so that it could not be used be used to determine radiographic grading of knee OA. (figure 3)

Discussions

The degenerative concept of OA view changes in OA as process of wear and tear. Long time usage and exaggeration will wear out the joint. Following the recurring process, osteophyte was formed as a response of bone repara-

Table 1. Description according to level CRP and radiographic grading at the sample

Radiographic Grading	Number of Samples	Level of CRP (mg/dl)			
		Minimum	Maximum	Mean	Std. Deviation
Grade < 3	28 (43%)	0.2	1.0	0.54	0.23
Grade 3	22 (34%)	0.3	1.4	0.70	0.33
Grade 4	15 (23%)	0.3	1.3	0.80	0.26
Total	65 (100%)	0.2	1.4	0.65	0.29

tion. This concept is supported by the imbalance between clinic manifestation (pain) and instability of joint with the broken of structure of joint and radiographic changes.[7]

The inflammation concept occurred either as acute or chronic inflammatory response. The level of CRP will increase in response of inflammation process. Synovial fluid analysis will reveal increased number of leukocyte and level of protein, decreased viscosity, and also increased variety of proinflammatory mediator. Synovial histopathological examination will reveal severe synovitis, exact histopathological changes, and increased cytokine.[7]

In healthy people, change of bone matrix is a balanced process of synthesis and degeneration. Inflammatory response induced by enzymatic process will result in cartilage damage as a target of damage in pathogenesis of OA.[7] Inflammation is one among causes of pain in OA, may initiate early process of pathogenesis of OA (especially post traumatic OA), and may also be a result of OA that will eventually progress the joint degeneration.[7] Inflammation of synovial in OA will increase IL-1 and TNF α, leading to induction of NO and production of metalloproteinase. IL-1 and biomechanical load in joint also induce catabolic receptors of cytokine. Binding of IL-6 and TNF-α to receptors in cartilage will result in further damage.[13]

CRP is an acute phase protein, which reflect a measure of the acute-phase response and can be used as early and preclinical marker of inflammation that was stimulated by certain cytokine (TNFα, IL-1, IL-6), resulting in enhancement of CRP by hepatocytes.[13]

The result of this study support the research carried out by Spector et al. in which was showed that the level of CRP were higher in women with Kellgren-Lawrence grade 2+ knee OA.[13] It is also in accordant with the research conducted by Takahashi et al.[11] which showed that there was correlation between radiographic grading and biochemical markers for arthritis of knee OA such as level of CRP.

Conclusions

There is no correlation between level of CRP and radiographic grading of knee OA, although in the low grade OA shows the weak correlation statistically. We propose the need of further study with larger number of samples and cohort study to see the progressivity of knee OA in association with increased of the level of CRP.

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